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(54) Title: APPARATUS FOR THE DETECTION OF VOLATILE AMINES

(57) Abstract

Apparatus for detecting the presence of volatile amines in a sample is disclosed. The apparatus has a receptacle (6, 40) containing a test composition. A swab (10, 16, 58) brings a sample into contact with the test composition and an indicator substance (30, 44) is arranged to detect vapour arising as a result of reaction of the sample with the test composition and to change colour if said vapour contains volatile amines. The apparatus can be used in the diagnosis of bacterial vaginosis.

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Title of the Invention

APPARATUS FOR THE DETECTION OF VOLATILE AMINES

Field of the Invention

The present invention relates to a diagnostic apparatus and method suitable for the detection of volatile amines.

Background to the Invention

Research which has been carried out in recent years indicates that a condition known as bacterial vaginosis (BV) is associated with volatile amines, particularly trimethyl amines which, when released, give a strong fishy odour. One test which is currently available to identify these volatile amines is to put some vaginal fluid on a slide with normal saline solution and then add potassium hydroxide. The hydroxide drives off the volatile amine and a strong fishy odour is released. A diagnostic device for carrying out a simple test of a similar nature is described in GB 2199944. This devic comprises a test tube containing an alkaline medium and a swab. The swab is placed in contact with vaginal fluid and then inserted into the alkaline medium in the test tube. The presence of volatile amines is detected by smell through a window or opening in the side of the test tube. While this device has resulted in major improvements in the ease of diagnosis of BV, there is a major disadvantage of th technique in that the detection of the volatile amines is subjective, difficult to standardise and unpleasant.

The present invention seeks to provide a diagnostic device and method which does not suffer from these disadvantages.

Summary of the Invention

According to the pr sent inv ntion there is provided an apparatus for det cting the presence of volatile amines in a

sample, the apparatus comprising a receptacle containing a test composition, means for r taining th sample in contact with the test composition and indicator means arranged to detect vapour arising as a result of reaction of the sample with the test composition and adapted to change colour if said vapour contains volatile amines, the test composition comprising a substance for driving out of solution any volatile amines present in the sample.

In the preferred embodiment, the test composition also comprises a second substance for trapping any ammonia from the sample to avoid the ammonia making contact with the indicator means.

Thus, the present invention provides an apparatus for detecting the presence of volatile amines, important in diagnosing BV, without the requirement to carry out the rather unpleasant "sniff test" required with the prior art device. The conversion of the detection of volatile amines from a test by smell to a test by colour change is not simple. Preferably the first substance is an alkali. In the reaction of the sample with an alkali, ammonia is produced from ammonium salts naturally present in body fluids. The nose is more sensitive to the vapour of amines than to ammonia. However, most chemical indicators capable of detecting one will also detect the other so that false positives could arise. The present inventors have thus provided in the preferred embodiment not only a substance to drive off the volatile amines for detection by the indicator means but also a substance to trap the ammonia.

In one embodiment, the first and second substances are pr vided by an alkaline solution of dipotassium t traiodom rcurate. The potassium tetraiodomercurate can b used as an ammonia trap sinc it reacts with ammonia to give a precipitat of complex ions. Thus, th ammonia is not driven off with the volatile amines so that the danger of false

positives is avoided. Dipotassium tetraiodomercurate can be used in a concentration of 65 grams per litr of solution.

The presence of volatile amines causes a change in pH. A wide range of pH indicator dyes can be selected as the indicator substance. The indicator substance or substances should be sensitive in the appropriate pH region to small changes in pH. The colour change of the indicator should be detected easily by eye, even by users with visual impairments such as colour blindness. The indicator dye should of course have properties which render it suitable for incorporation into a manufactured device, for example it should be chemically stable. One preferred indicator means comprises nitrazine yellow which changes its colour from yellow to blue in the presence of trimethyl amine and other amines at a pH of about 6.5. Nitrazine yellow is particularly sensitive at this pH and will change its colour with only a small change in pH (from 6.0 - 7.2).

In a clinical application, the apparatus can be used to carry out the test in an automated fashion. However, since the diagnosis of BV is more commonly the province of General Practices, what is mainly required is a diagnostic device which is easy and safe to use with a reasonable degree of indication accuracy. To that extent, the present invention provides in one aspect a diagnostic device comprising a first part defining the receptacle containing the test composition; means for supporting a swab carrying the sample so that the sample is in contact with the test composition; and a second part capable of engagement with the first part and carrying the indicator means such that engagement of the second part with the first part closes off the receptacle and causes the swab to come into contact with the test composition, the indicator m ans being visibl in use of the devic .

Pref rably th first part comprises a base having an upstanding wall defining said receptacle and a guide constituting the swab supporting means and the second part has

a ledge for engaging said upstanding wall, an upper surface carrying the indicator means and a lower surface for applying pressure to the swab to bring it into contact with the test composition in the receptacle, there being at least one passageway for enabling vapour emitted during a test to pass from the lower surface to the upper surface and thereby to contact the indicator means.

The second part can comprise an indicator cap assembly having a cap body defining the ledge, an indicator pad constituting the indicator means said pad being arranged between the upper surface of the cap assembly and a mesh. Preferably there is a gas permeable membrane between the upper surface of the cap assembly and the indicator pad.

In a second embodiment of the present invention, there is provided a diagnostic device comprising a body part containing the test composition in a manner such that the test composition can be caused to move relative to the body part by the insertion of a swab carrying the sample, and an indicator part containing the indicator means and arranged such that when the test composition has been moved by the swab carrying the sample relative to the body part, vapour released therefrom is brought into contact with the indicator means.

Preferably the swab is supported by a swab stick which carries a seal defining behind the swab and with the body part a reaction chamber.

It has been found by the inventors that swabs having swab sticks made of Dacron (Registered Trade Mark) are better than the more conventional swabs with wooden swab sticks.

The present inv ntion also provides a method of carrying out a test for d tecting the pres nce of volatil amines, the method comprising:

taking a sample of body fluid from a patient,

placing the sample in contact with a test composition comprising a first substance to drive volatil amines out of solution and a second substance to absorb ammonia, and

detecting the colour change of an indicator means placed in contact with vapour driven off from the sample by the first substance.

The invention also provides a method of diagnosing bacterial vaginosis by carrying out the steps of the above defined method.

For a better understanding of the present invention, and t show how the same may be carried into effect reference will now be made by way of example to the accompanying drawings.

Brief description of the drawings

Figure 1 is a section through a base part of a first embodiment of a diagnostic device;

Figure 2 is a section through an indicator cap assembley of a diagnostic device;

Figure 3 is a view of an indicator cap assembly from below;

Figure 4 is a view of an indicator cap assembly from above;

Figure 5 is a view from above of a diagnostic device with its swab in a test position;

Figure 6 is a section taken along the lines VI-VI in Figure 5;

Figure 7 is a view of the indicator cap assembly along the line of the swab test position;

Figure 8 is a view of the diagnostic device from abov with the indicator cap assembly in plac ;

Figur 9 is a section taken along the line IX-IX in Figure 8;

Figure 10 is a view of the diagnostic device with the swab in th test position vi wed along th line of th swab stick t st position;

Figure 11 is a view of the diagnostic device showing the appearanc f r a negativ test;

Figure 12 is a view of the diagnostic device showing the appearance for a positive test;

Figure 13 is a longitudinal section through a second embodiment of the present invention;

Figure 14 illustrates a swab for use in the second embodiment of the present invention;

Figures 15a to 15c demonstrate the use of the second embodiment of the present invention;

Figure 16 is a sketch illustrating an apparatus used to carry out tests in accordance with the present invention;

Figure 17 is a section through a reaction tube forming part of an apparatus in accordance with another embodiment of the present invention;

Figure 18 is a section through a closure assembly for cooperation with the reaction tube of Figure 17; and

Figures 19a to 19f illustrate use of the embodiment of Figures 17 and 18.

Description of the preferred embodiment

A diagnostic device in accordance with a preferred embodiment of the present invention will now be described with reference to the drawings.

In a first embodiment, a diagnostic device comprises a base part illustrated in Figure 1 and an indicator cap assembly illustrated in Figures 2 to 4. The base part comprises a base support 2 having an upstanding wall 4 which defines a receptacle or reaction chamber 6. The base part also has a further upstanding support 8 for supporting a swab stick 10, the upstanding support 8 and the wall 4 of the reaction chamber 6 each defining r spective swab stick guide walls 12 and retaining slots 14. The swab stick 10 carries a swab head 16 and th arrangem nt of the guide walls 12 and retaining slots 14 is such that wh n the swab stick 10 is supported ther by th swab head 16 lies within the reaction chamber 6.

The reaction chamber has an absorbent matrix 18 secured within the wall 4 of the reaction chamber 6 by an O-ring seal 20. The absorbent matrix can take the form of a sponge or similar material and is impregnated with a chemical composition for carrying out a diagnostic test. This composition will be described in more detail hereinafter.

The indicator cap assembly comprises a body 22 having an upper annular ring 24 which has a lower surface defining a ledge 24a and an upper surface supporting a ring 26 of adhesive. The adhesive secures a gas-permeable membrane 28 across an upper surface 29 of the body 22. An indicator pad 30 is secured between the gas-permeable membrane 28 and a mesh 32 also secured by the adhesive 26. The body 22 defines four centrally located passageways 34 (seen most clearly in Figure 3) extending from a lower surface 31 of the body 22 to th upper surface 29 for a purpose to be described hereinafter. The body 22 also has a swab stick retaining lug 36.

Figure 4 shows the test cap indicator assembly from above illustrating the adhesive 26, the mesh 32 and the indicator pad 30 viewed through the mesh.

Figure 5 is a plan view of the base part with the swab in position for a test. The swab stick 10 is supported in th slots 14 and between the guide walls 12 (see Figure 6). The swab head 16 then sits in the surface of the absorbent matrix 18. Figure 7 shows the indicator cap assembly when viewed along the swab stick 10. In particular, the swab retaining lug 36 can readily be seen.

Figure 8 to 10 show the diagnostic device in the process of a test. Figure 9 is a s ction through the d vic showing th swab 10 supported by the retaining slots 14 with th swab head pushed into the absorbent matrix 18 by the indicator cap assembly. The indicator cap assembly seals th reaction chamber 6 by virtue of the annular ledge 24a engaging the wall 4 of th r action chamber 6. The passages 34 allow the

release of vapour resulting from the test to pass through th gas-permeable membran 28 to the indicator pad 30. As can be seen most clearly in Figure 10, the swab stick retaining lug 36 sits neatly in the guide walls 12 defining the slot 14.

The absorbent matrix 18 contains an alkaline solution of dipotassium tetraiodomercurate which provides a substance t drive off volatile amines, namely potassium hydroxide and a substance, potassium tetraiodomercurate, which traps and retains any ammonia present in the sample to prevent it from causing the indicator to give a false positive. The matrix 18 can comprise any absorbent material, such as gauze, impregnated with the chemicals in solution and then dried. The matrix 18 must thus be rehydrated before use. The indicator pad 30 comprises an indicator selected to change colour around the pH range of a contaminated sample, namely 5. In the preferred embodiment, nitrazine yellow is used which changes colour from yellow to blue as a result of the change in pH caused by the presence of trimethyl amine.

The device is supplied ready for use with the base part and indicator cap assembly secured to one another and with a separate sterile pack containing a swab. The swab is used to take a sample, the indicator cap assembly is removed from th base part, and the matrix 18 is wetted with water to rehydrate it. The indicator pad is also wetted by applying water through the mesh. The swab is then placed on the base part as shown in Figures 5 and 6. The indicator cap assembly is then immediately replaced onto the base part and pressed into position to squash the swab head 16 into the reaction chamber 6. Vapour driven off by the reaction of the test composition with the sample enters the passageways 34, passes through th gas permeable membrane and contacts the indicator pad. The colour of the indicator pad is th n noted. Figur 11 shows the assembly when ther is no change in colour of the pad and Figure 12 shows the assembly when the pad has changed in colour from y llow to blue, thus indicating a positiv result.

The second embodiment of th present invention will now be described with reference to Figures 13 to 15c. Figure 13 illustrates an indicator tube assembly in section, the assembly comprising a tube body 40 sealed at one end thereof by a cap 42 and at the other end thereof by an indicator assembly 44. The indicator assembly takes the form of a closure device having a tubular part 46 for fitting over the open end of the tube body 40 and a conical part 48. The conical part 48 houses a fixed plug 50 of a firm gel which contains the indicator chemicals. A gas permeable membrane 52 is provided extending across the conical part 48. The tube body 40 also houses a plug 54 of soft (but not runny) gel, movable along the tube body 40. The plug 54 of gel in the tube body contains the test composition, namely a first substance for driving off the volatile amines and a second substance for trapping any ammonia released as a result of reaction of the first substance with body fluids. The substances can be provided by a solution as in the first embodiment of the present invention. Likewise, the indicator chemicals in the plug 50 of gel in the conical part of th indicator assembly 44 can comprise nitrazine yellow.

The diagnostic device also comprises a swab assembly comprising a swab stick 56 carrying a swab head 58. The swab stick also carries an O-ring piston seal 60 the purpose of which will be described hereinafter. The piston seal 60 is located just behind the swab head 58.

Use of the diagnostic device in accordance with the second embodiment of the present invention will now be described with reference to Figures 15a to 15c.

The cap 42 is removed fr m the test tube body, the swab 58 is us d to tak a sample of body fluid and is then insert d into the open end of the tube body 40. Th swab is push d to the left in Figure 15a until it nters the plug 54 containing the test composition. The swab head is push d into the plug and causes th plug to mov with it towards the oth r end of th

tube body. As shown in Figure 15c, th swab head immersed in the plug 54 ev ntually abuts the gas permeable membrane 52. Vapours released from the reaction of the components of the body fluid with the reagents in the test composition pass through the gas permeable membrane and contact the indicator chemicals in the plug 50. The gas permeable membrane allows the swab head to come close to the plug 50 without the test composition of the plug 54 affecting the indicator chemicals. The plug 50 then turns colour to indicate a positive reaction or shows no change in colour if the test is negative.

The O-ring piston seal 60 protects the user from coming into contact with the alkali reagent in the plug 54. The piston seal also ensures that the amine vapour is contained in a test chamber defined at the end of the tube body by the indicator assembly conical part and the piston ring seal. This allows for increased sensitivity and speed of the test. It also allows hygenic disposal of the assembly after use without release of the amine vapour and its associated smell.

The conical part can be provided at its tip with a lens to magnify the indicator gel 50 for ease of use.

There follows the results of experiments demonstrating the effectiveness of the ammonia trap. The experiments wer carried out using a simplified testing device as outlined below with reference to Figure 16.

A test sample was placed onto a swab and the swab was then exposed to an ammonia trap or to a control solution (no ammonia trap). The test result was the time taken to change the colour of a pH indicator pad and this was recorded.

The swab illustrated in Figure 16 is th same as that in Figure 14 but is supplied initially without the seal 60. After use, the used swab is placed head up in a container ready for testing. The seal is pushed onto the swab handle up to the base of the swab and secur d with a small drop of

superglue. A drop (0.1ml) of wetting reagent was put on a petri dish lid. Fine (dry) tweezers were used to take an indicator disc and wet it. Excess wetting was removed by touching the disc on the surface of filter paper or the like. The wetted disc was stuck on the inside wall of a syringe barrel 72 about 3mm inside the open end as shown in Figure 16 with the indicator disc being denoted by reference numeral 70. Holding the syringe barrel 72 upright, with the indicator disc 70 at the top, the swab is inserted into the bottom end of the syringe barrel and pushed halfway up. Using a pipette, 0.05ml of solution with an ammonia trap or control solution is dispensed on top of the swab as indicated by arrow R in Figur 16. The swab handle 56 was twisted between thumb and forefinger a couple of times (to help the solution penetrate the swab) whilst pushing the swab further up the barrel until its tip is near but not touching the indicator disc 70. The open end 74 of the syringe barrel was then quickly sealed with a sealing disc 76.

The test sample and the ammonia trap were added in 50ul volumes. Trimethylamine was used as the hydrochloride, ammonia was used as ammonium chloride. The ammonia trap used was an alkaline solution of dipotassium tetraiodomercurate, 65 g/L. In the control experiments (no ammonia trap) a solution of 50 mM sodium hydroxide was used instead.

Results

Expt No.	Test Sample	Conc. of Sample	Ammonia Trap	Test Result (time in minutes for indicator pad to change colour)
1	Trimethylamine	1 mM	Yes	3
2	Ammonia	1 mM	Y s	25
3	Trimethylamine	1 mM	Y s	3
4	Trimethylamine	0.1 mM	Yes	6
5	Ammonia	1 mM	Yes	23
6	Ammonia	10 mM	Yes	13

7	Trimethylamine	0.1 mM	N	6
8	Ammonia	0.1 mM	No	8
9	Trimethylamine	0.1 mM	No	4
10	Ammonia	0.1 mM	No	7
11	Trimethylamine	0.1 mM	Yes	6
12	Ammonia	1 mM	Yes	>30
13	Ammonia	1 mM	No	2.5
14	Ammonia	1 mM	Yes	30
15	Trimethylamine	1 mM	Yes	3
16	Trimethylamine	0.1 mM	Yes	6

Further appraisal of the ammonia-trapping efficiency of dipotassium tetraiodomercurate reagent was obtained by immersing ammonium chloride-impregnated swabs in 1 ml dipotassium tetraiodomercurate or sodium hydroxide (50mM) solution contained in plastic Eppendorf tubes (2.25ml) which had moistened indicator (nitrazine yellow) discs stuck to their inside surface, above the alkali solution. The tubes were immediately sealed with their screw-caps which were drilled to accommodate the swab shafts.

Test Sample (on swab)	Test Sample Conc.	Ammonia Trap	Result (time in minutes to change indicator pad)
Ammonia	50 mM	Yes	>44
Trimethylamine	1 mM	Yes	1.5
Ammonia	1 mM	No	1.5
Ammonia	50 mM	Yes	>30
Ammonia	100 mM	Y s	2

Th results show that in the absence of the ammonia trap, samples which contain trimethylamine or ammonia r act quickly and change the colour of the indicator disc within 4 to 8 minutes (experiments 7 to 10). Experiments 8 and 10 show that

even low concentrations of ammonia in the clinical sample could caus a false positive test result to be obtained.

However, when the ammonia trap was used trimethylamine still reacted within 6 minutes (experiments 1,3,4,11,15 and 16) as it was expected to do but ammonia now gave a much slower response. The response to ammonia now took from 13 to 30 minutes depending on ammonia concentration (experiments 2,5,6,12,14). Thus, if the response time is set at 8 minutes, all the trimethylamine samples would give positive results with or without the ammonia trap. The ammonia samples however would only give negative results if the ammonia trap was in use.

Reference will now be made to Figures 17, 18 and 19a to 19f to describe a further embodiment of the present invention. Figure 17 shows a reaction tube 81 which contains an absorbant pad 82 containing an alkali reagent and an ammonia trap as discussed above with reference to the first and second embodiments of the invention. Reference numeral 83 denotes a cap for the reaction tube 81.

Figure 18 illustrates a closure and operating assembly for the reaction tube of Figure 17. The assembly comprises a cylindrical piston body 86 having an upper annular part which engages the top of the reaction tube in use and which is denoted by reference numeral 86a. The piston body 86 carries at its lower end two piston sealing rings 99.

There is a passageway 100b extending centrally of the piston body through which a swab handle can pass in use as described later. There is also a gas transfer channel 92 which extends al ng the piston body and which is surrounded at its upper end by a pointed annulus 93.

Th closur and operating assembly also compris s a transpar nt cylindrical indicator cap 87. Th cap 87 has on its underside a locating ring 94 which engages a corresponding

locating circular recess 95 in the upper face of the annular part 86a of the piston body 86. The cap 87 defines an indicator solution chamber 96 which contains indicator solution illustrated by reference numeral 89. The indicator solution chamber 96 has in its upper end a vent hole 88 sealed by a vent closure 88a. It has at its lower end a narrow capillary access port 97. The access port 97 is sealed by a membrane 90.

A passageway 100a extends through the cap 87 in alignment with the passageway 100b of the piston body 86. These passageways 100a and 100b receive a swab handle 85 carrying a swab 84.

Use of the device will now be described with reference to Figures 19a to 19f. A sample is taken from a patient using the closure assembly as illustrated in Figure 18. The cap 83 is then removed from the reaction tube 81 and the closure assembly with the patient sample is placed into the reaction tube 81 so as to fully immerse the swab 84 in the absorbant pad 82 and to simultaneously locate the piston body 86 into the reaction tube 81 as illustrated in Figure 19a. The locating ring 94 of the cap 87 is engaged by the locating recess 95 of the piston body 86 in such a fashion as to leave a gap 91 between the upper face of the annular part of th piston body and the lower face of the indicator cap 87. In this position, the pointed annulus 93 touches but does not penetrate the membrane 90 of the indicator solution chamber 96.

Still in a vertical position, the indicator cap 87 is then snapped into the annular part 86a of the piston body 86 so that the pointed annulus 93 pierces the membrane 90 of the indicator solution chamber 96. This has the effect of connecting the gas transf r channel 92 within the piston body 86 to the narrow capillary acc ss port 97 of the indicator cap 87. This is illustrated in Figure 19b.

With the combined assembly still in a vertical position, the closure 88a for th v nt 88 is removed. This is illustrated in Figure 19c. The combined cap and piston assembly is then pushed slowly into the reaction tube 81 until it comes to rest so that all of the gas in the reaction tube 81 passes through the gas transfer channel 97 of the piston body 86, bubbles through the indicator solution 89 and then passes out through the vent 88. This is illustrates in Figure 19d. During this, the piston seals 99 contact in a fluid tight manner the inner walls of the reaction tube 81. Finally, the vent closure 88a is replaced on the vent 88 and the test is complete. This is shown in Figure 19e which illustrates a positive result where the indicator solution (which can be seen through the transparent indicator cap) has changed colour and in Figur 19f which indicates a negative result where the indicator solution has not changed colour.

This apparatus has the advantages mentioned above in relation to the other embodiments of the invention but in addition has the following features:

A sealed reaction chamber is formed which leaves a headspace for amine gas to collect above the liquid reaction area.

The device has a space for the amine gases to enter.

The operation of the mechanism of the device has th effect of forcing the gas to where it is required (namely t bubble through the indicator solution).

The gas in the headspace is forced into the gas transf r channel and passes through this so as to make good contact with a small volume of indicator fluid.

CLAIMS:

1. Apparatus for detecting the presence of volatile amines in a sample, the apparatus comprising a receptacle containing a test composition, means for retaining the sample in contact with the test composition and indicator means arranged to detect vapour arising as a result of reaction of the sample with the test composition and adapted to change colour if said vapour contains volatile amines, the test composition comprising a substance for driving out of solution any volatile amines present in the sample.

2. Apparatus according to claim 1 wherein the test composition also comprises a second substance for trapping any ammonia from the sample to avoid the ammonia making contact with the indicator means.

3. Apparatus according to claim 2 wherein the test composition comprises an alkaline solution of dipotassium tetraiodomercurate.

4. Apparatus according to claim 3 wherein the test composition is an alkaline solution of dipotassium tetraiodomercurate at a concentration of 65 grams per litre of solution.

5. Apparatus according to any preceding claim wherein the indicator means comprises a pH indicator substance, for example nitrazine yellow.

6. A diagnostic device for detecting the presence of volatile amines in a sample, the device comprising a first part defining a receptacle containing a test composition comprising a substance for driving out of solution any volatile amines present in the sample;

means for supporting a swab carrying a sample so that the sample is in contact with the test composition; and

a second part capable of engagement with the first part and carrying indicator means arranged to detect vapour arising as a result of reaction of the sample with the test composition and adapted to change colour if said vapour contains volatile amines, the device being such that engagement of the second part with the first part closes off the receptacle and causes a swab to come into contact with the test composition, the indicator means being visible in use of the device.

7. A diagnostic device according to claim 6 wherein th first part comprises a base having an upstanding wall defining said receptacle and a guide constituting the swab supporting means and the second part has a ledge for engaging said upstanding wall, an upper surface carrying the indicator means and a lower surface for applying pressure to the swab to bring it into contact with the test composition in the receptacle, there being at least one passageway for enabling said vapour emitted during a test to pass from the lower surface to the upper surface and thereby to contact the indicator means.

8. A diagnostic device according to claim 7 wherein the second part comprises an indicator cap assembly having a cap body defining the ledge, and indicator pad constituting th indicator means and being arranged between the upper surfac of the cap assembly and a mesh.

9. A diagnostic device according to claim 8 comprising a gas permeable membrane between the upper surface of the cap assembly and the indictor pad.

10. A diagnostic device according to claim 6 wherein the means for supporting a swab compris s a piston member defining a passageway for locating a swab handl and being movable r lative to the swab handle within the receptacle.

11. A diagnostic device according to claims 6 and 10 wh rein the second part defines a chamber housing indicator fluid constituting said indicator means, said chamber having an inlet capable of communication with gas in the receptacle via a passageway associated with the piston member.

12. A diagnostic device according to claim 11 wherein the inlet of the indicator fluid chamber is sealed by a penetrable membrane and wherein the piston body carries means for penetrating said membrane in use of the device.

13. A diagnostic device comprising a body part containing a test composition in a manner such that the test composition can be caused to move relative to the body part by the insertion of a swab carrying a sample, the test composition including a substance for driving out of solution any volatile amines present in the sample; and

an indicator part containing indicator means arranged to detect vapour arising as a result of reaction of the sample with the test composition and adapted to change colour if said vapour contains volatile amines, the indicator means being arranged such that when the test composition has been moved by the swab carrying the sample relative to the body part, vapour released therefrom is brought into contact with the indicator means.

14. A diagnostic device according to claim 13 wherein the swab is supported by a swab stick which carries a seal defining behind the swab and with the body part a reaction chamber.

15. A diagnostic device according to any of claims 6 to 14 wherein the test composition also comprises a substance to absorb ammonia.

16. A method of carrying out a test for detecting the presence of volatile amines, the method comprising:

taking a sample of body fluid from a patient;

placing the sample in contact with a test composition comprising a first substance to drive volatile amines out of solution and a second substance to absorb ammonia; and

detecting the colour change of an indicator means placed in contact with vapour driven off from the sample by the first substance.

17. A method of diagnosing baterial vaginosis by carrying out the steps of the method according to claim 16.

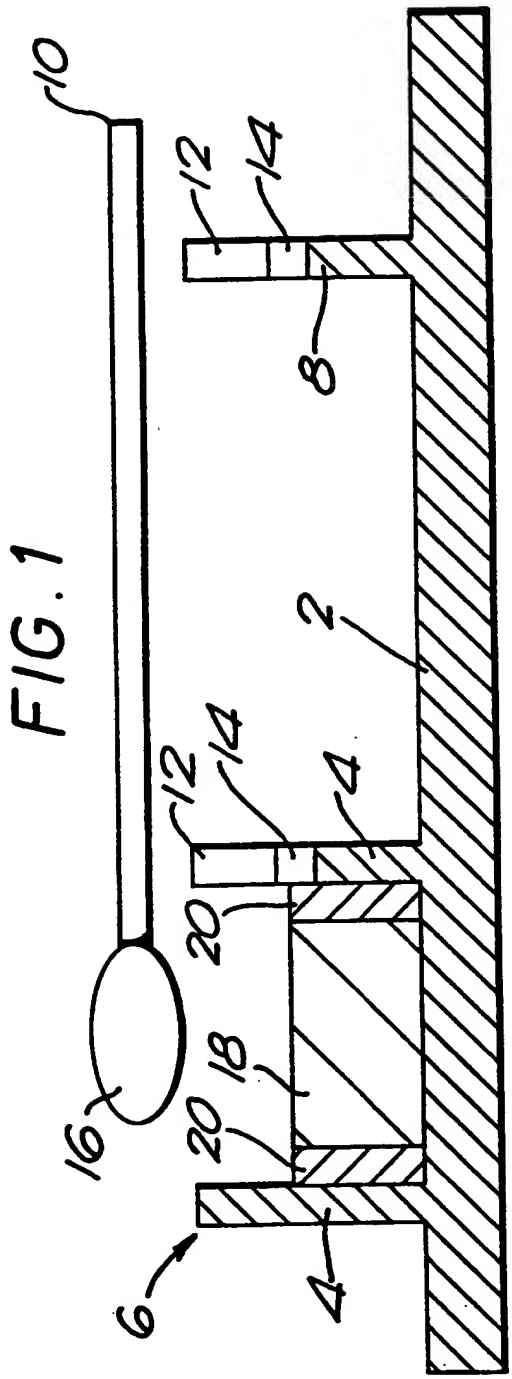


FIG. 1

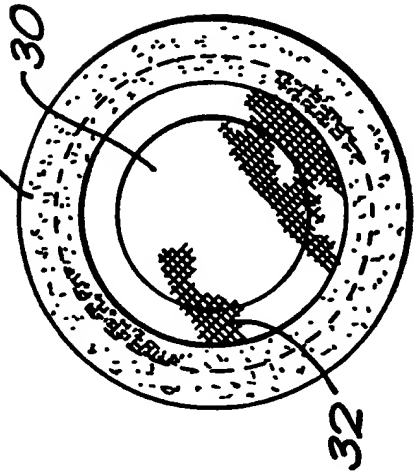


FIG. 4

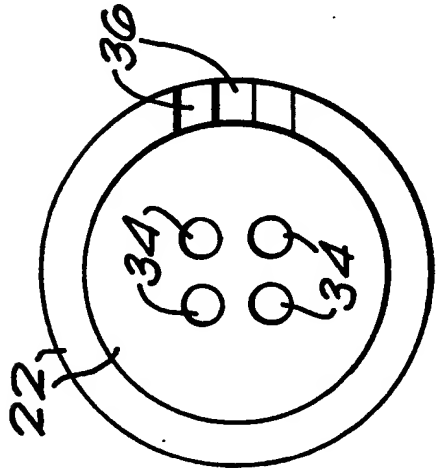


FIG. 3

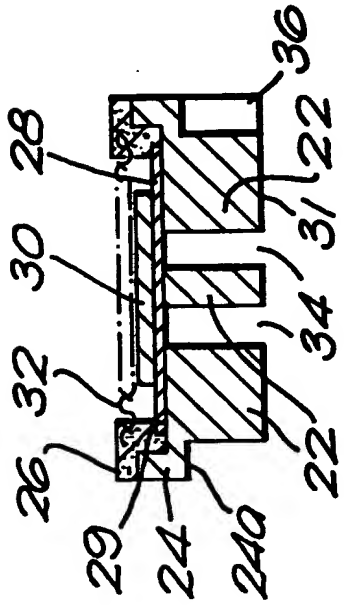


FIG. 2

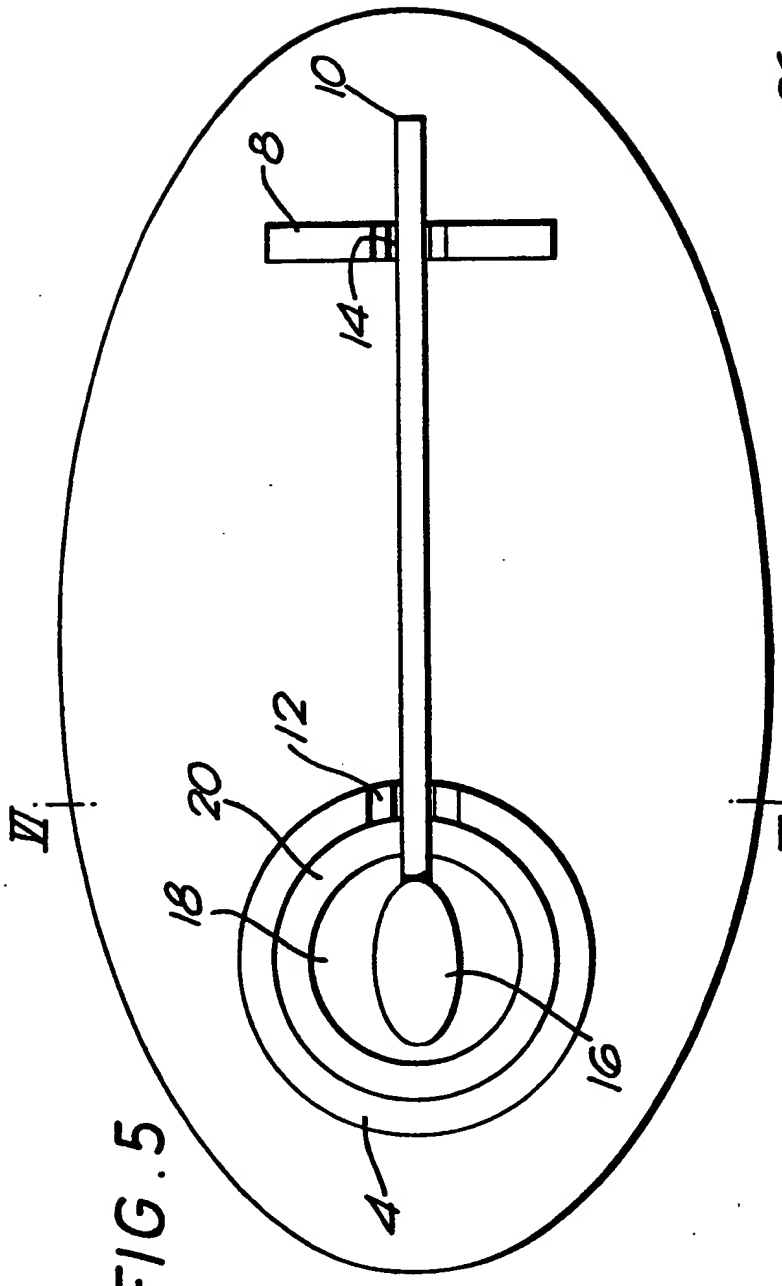


FIG. 5

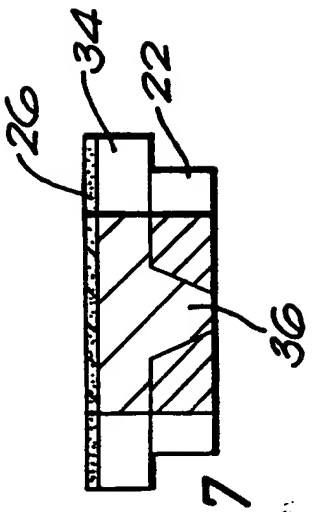


FIG. 7

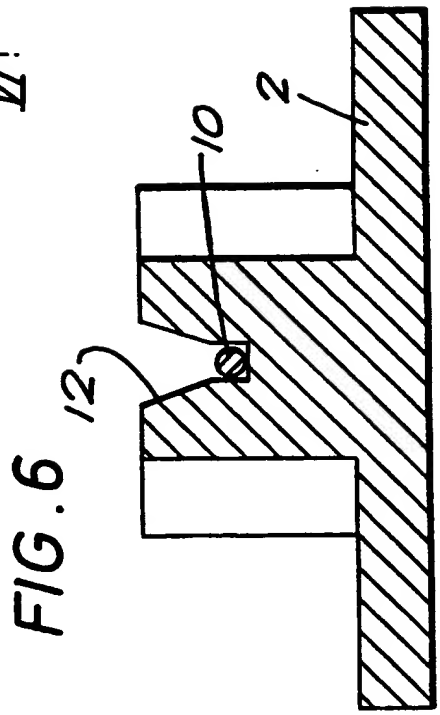


FIG. 6

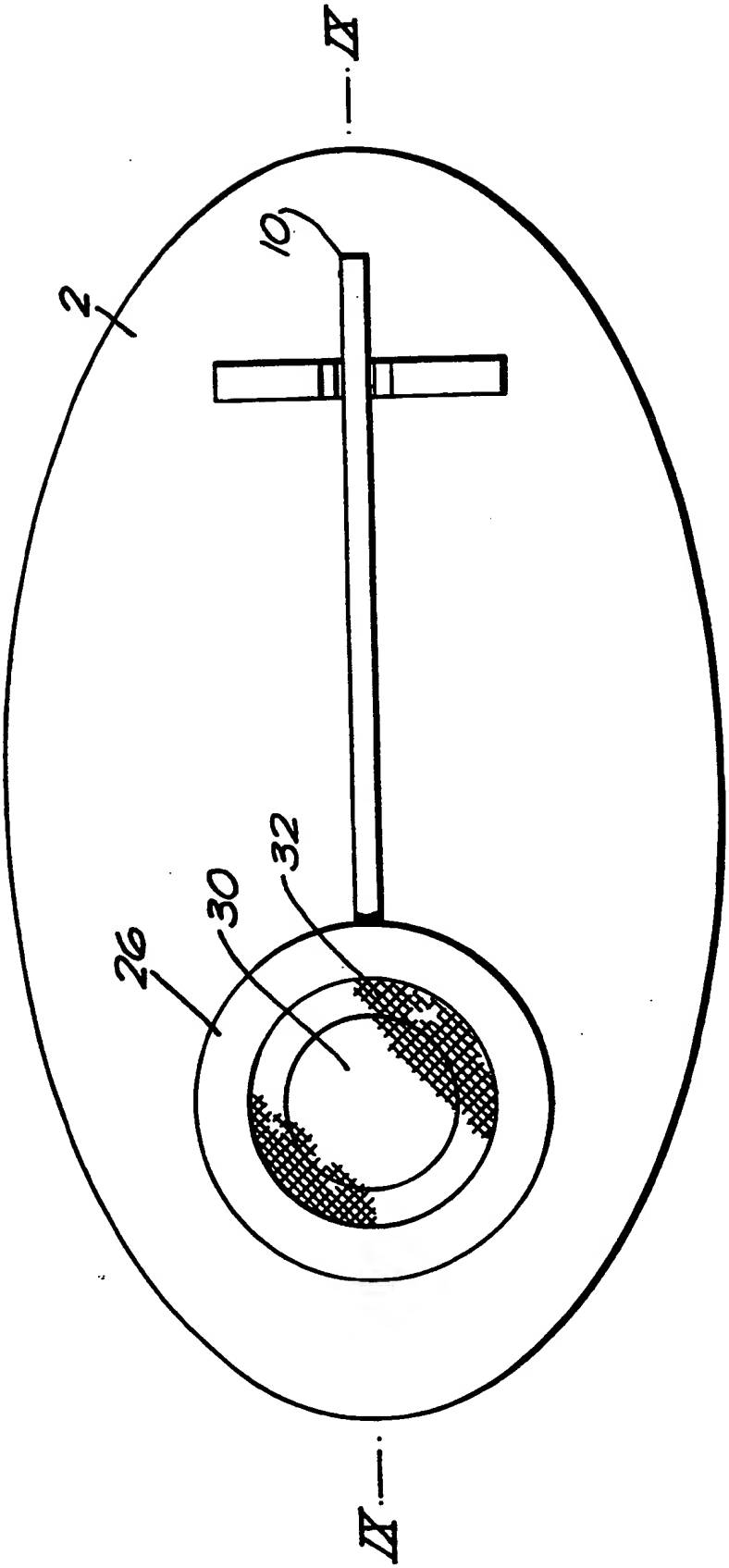


FIG. 8

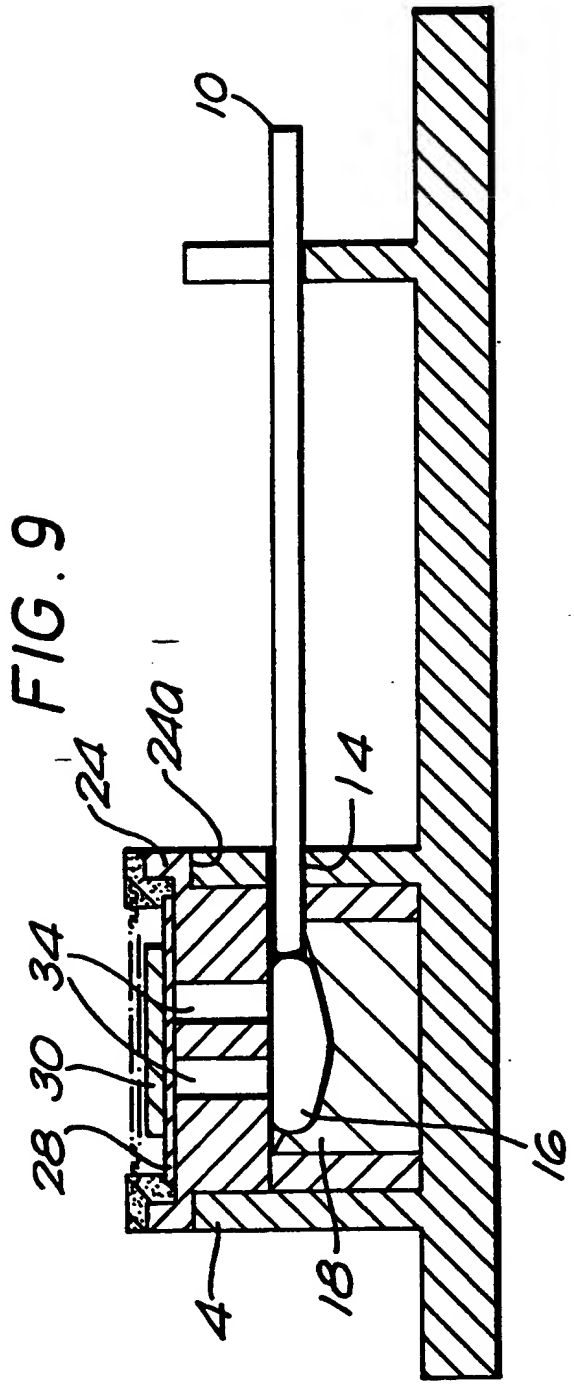


FIG. 9

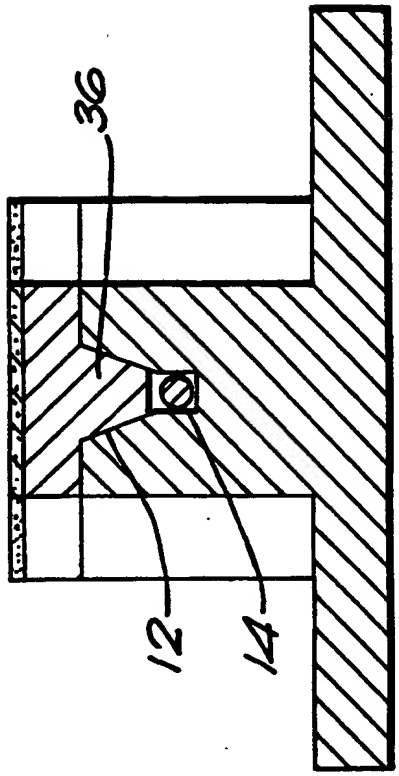


FIG. 10

FIG. 11

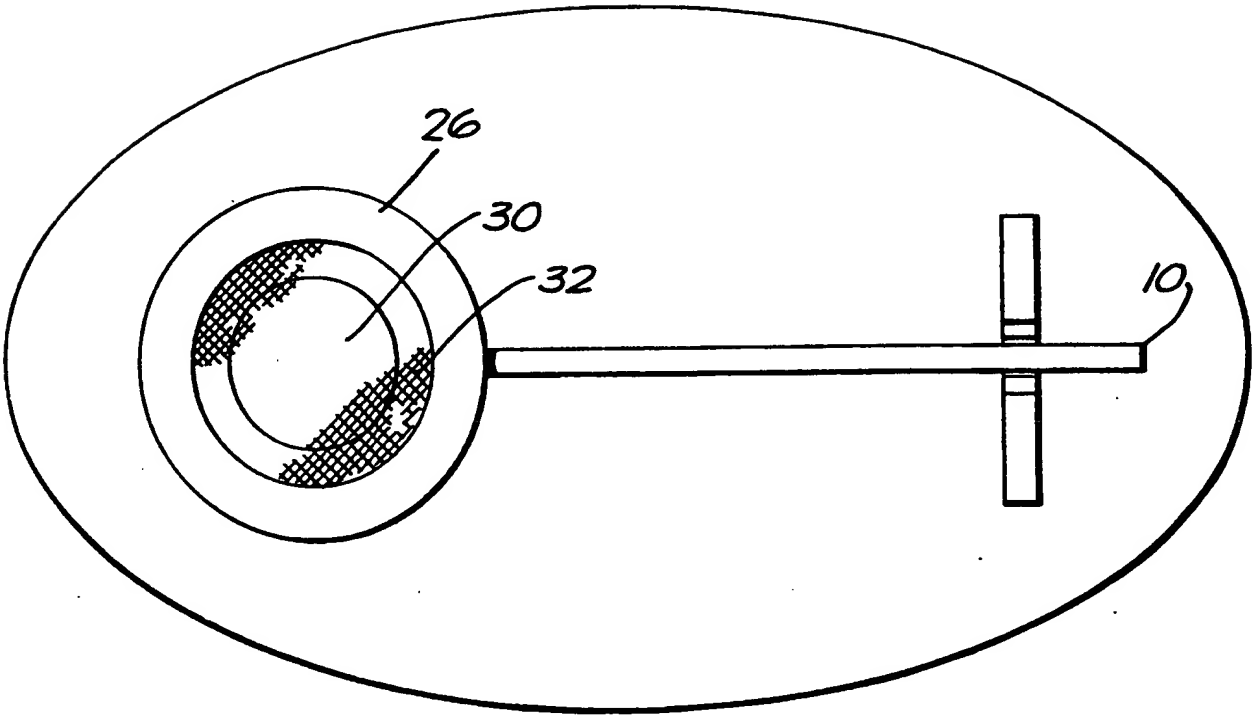
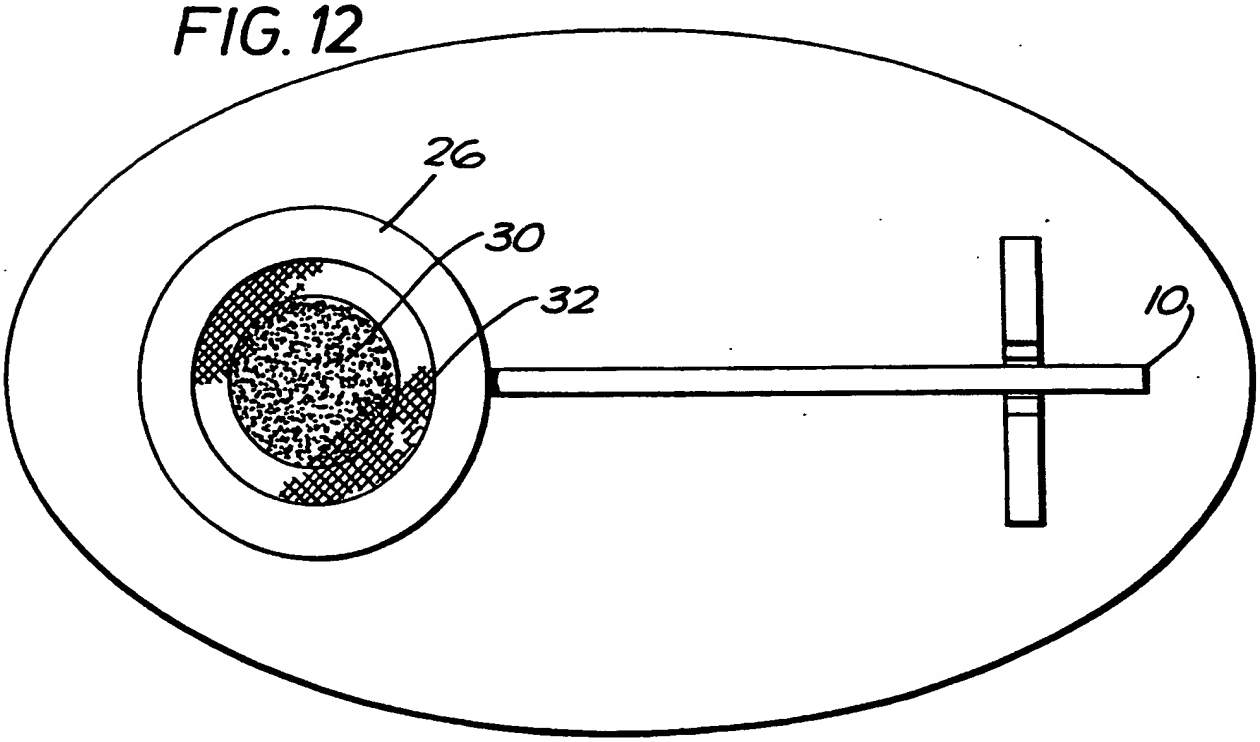


FIG. 12



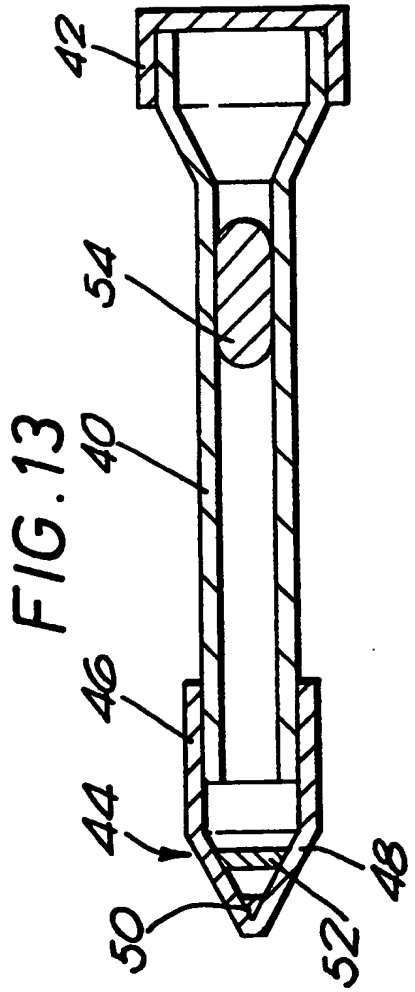


FIG. 13

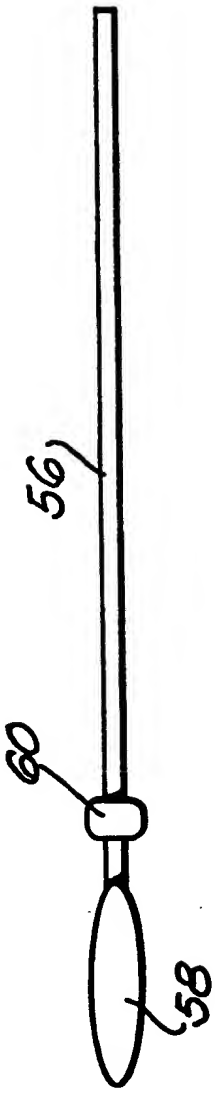


FIG. 14

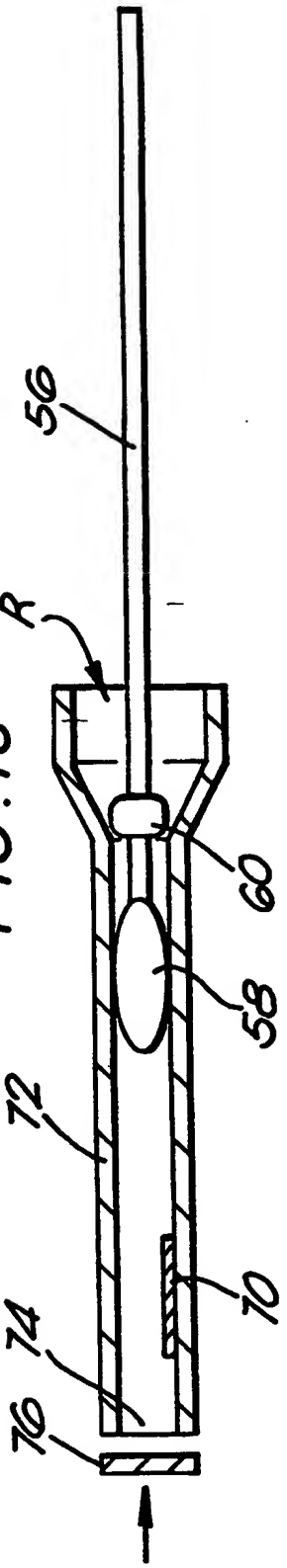


FIG. 16

FIG. 15a

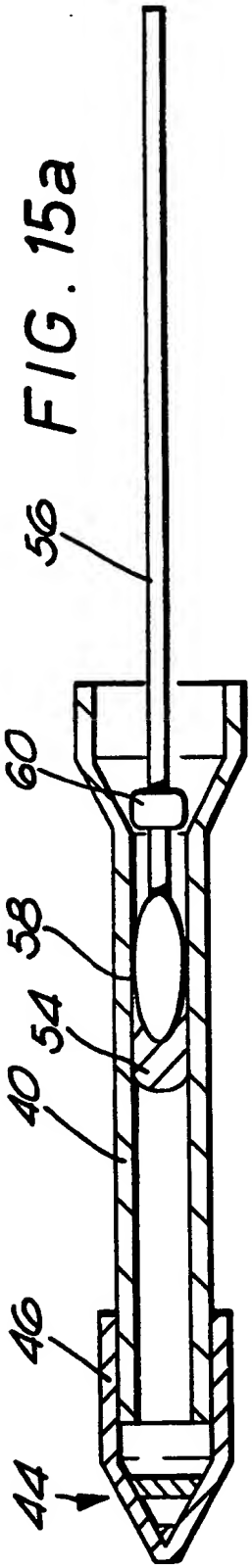


FIG. 15b

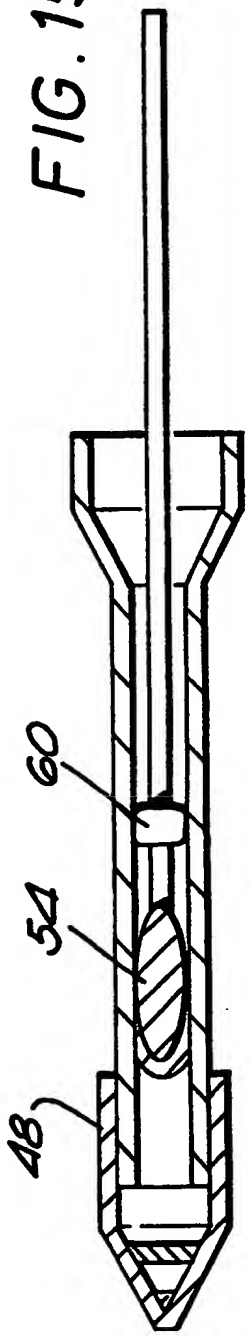
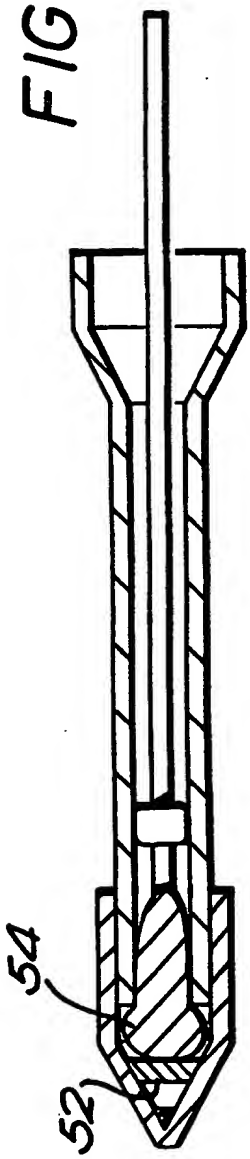


FIG. 15c



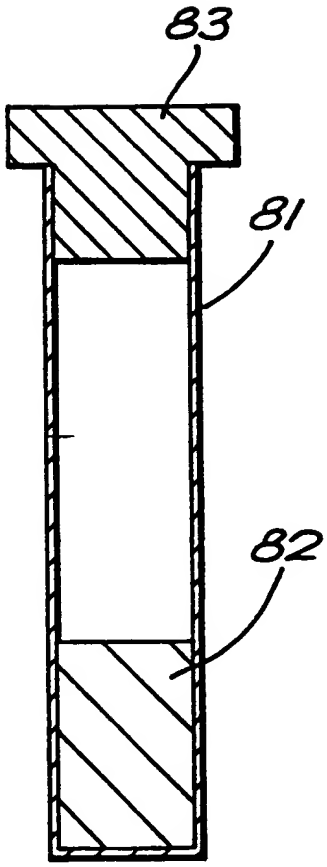


FIG. 17

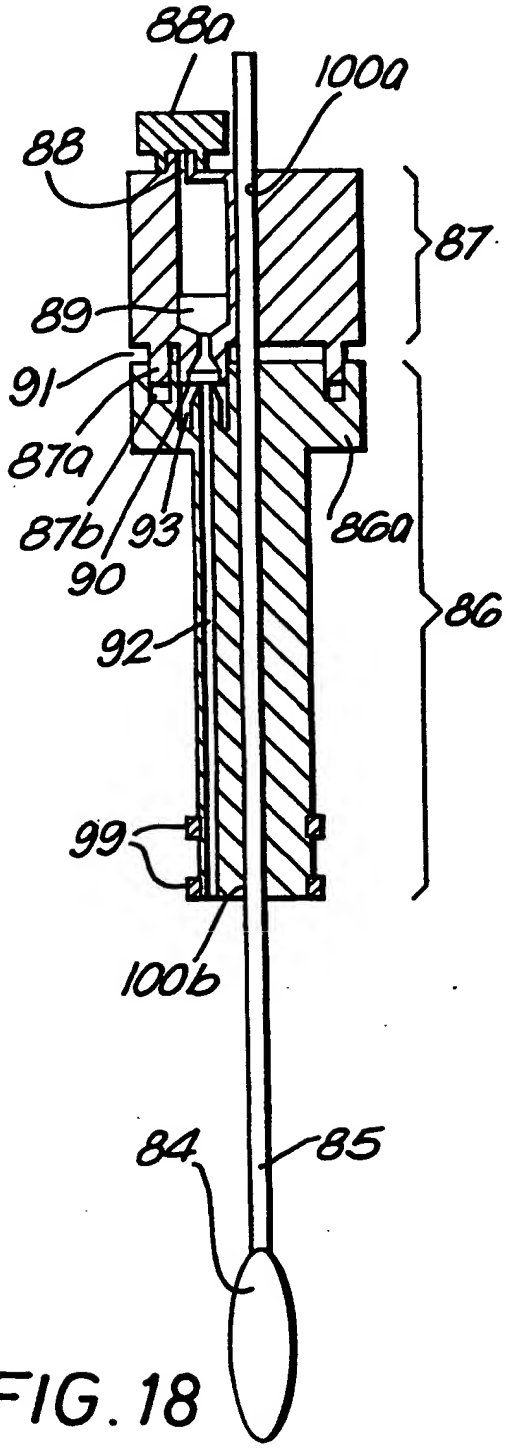


FIG. 18

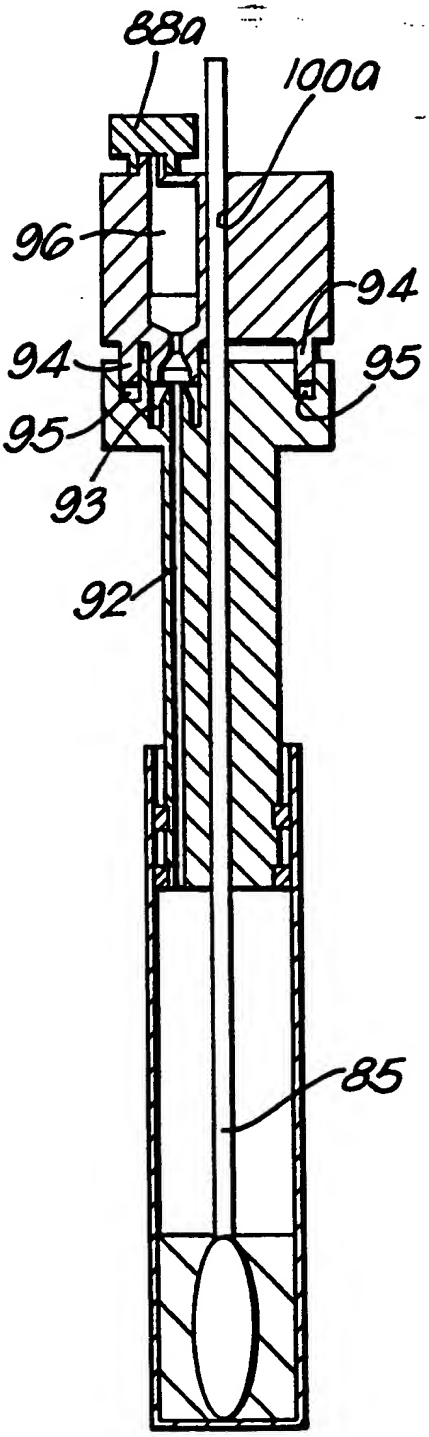


FIG. 19a

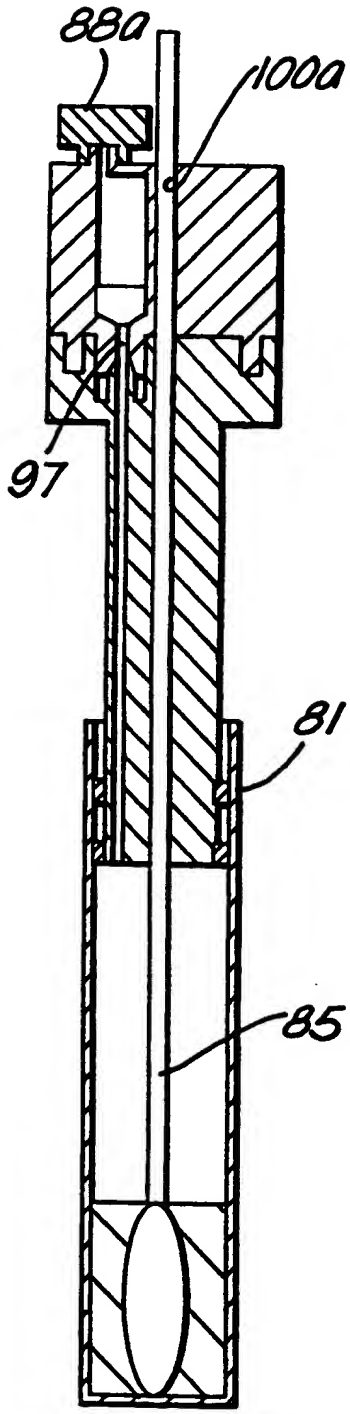


FIG. 19b

FIG. 19c

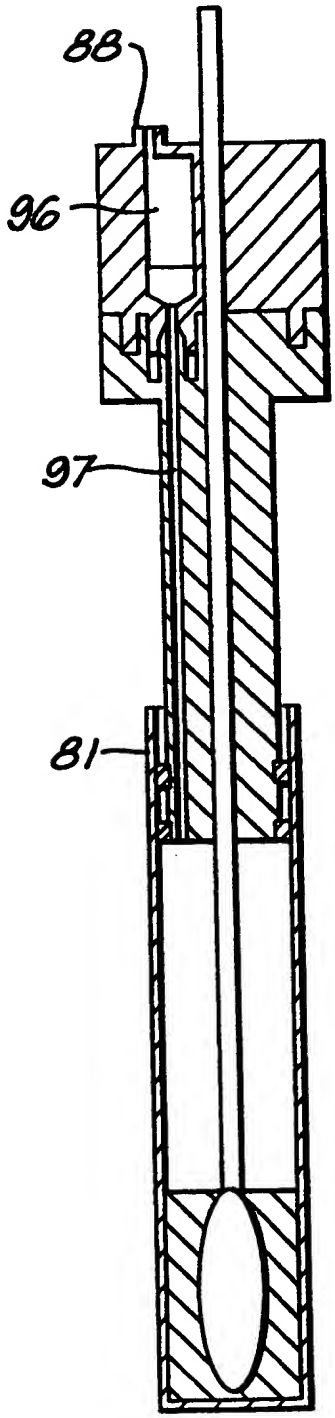


FIG. 19d

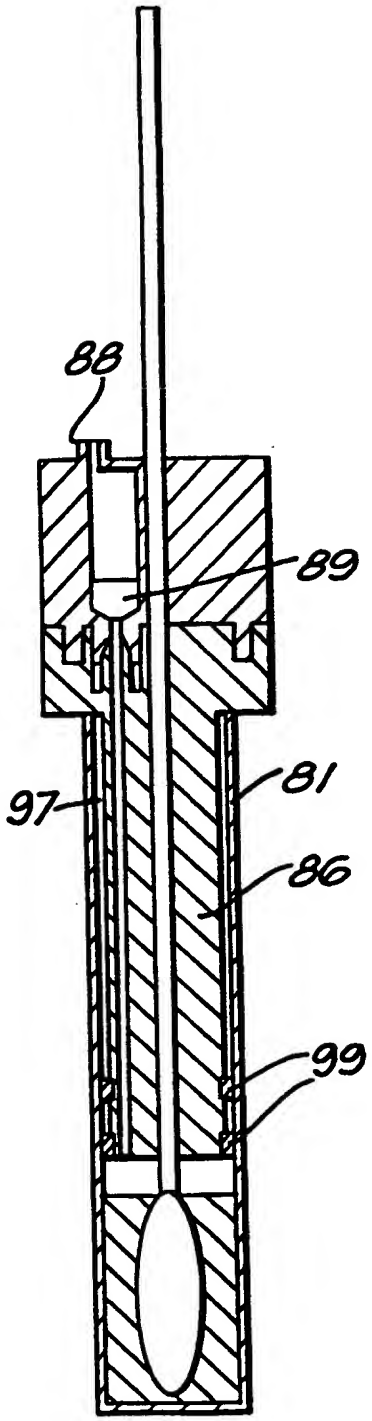


FIG. 19e

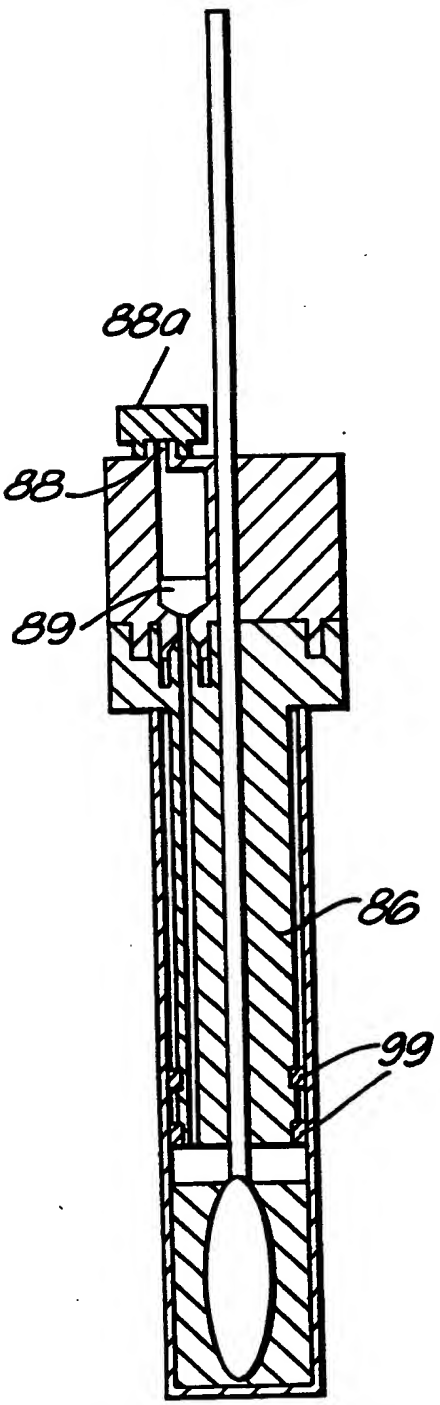
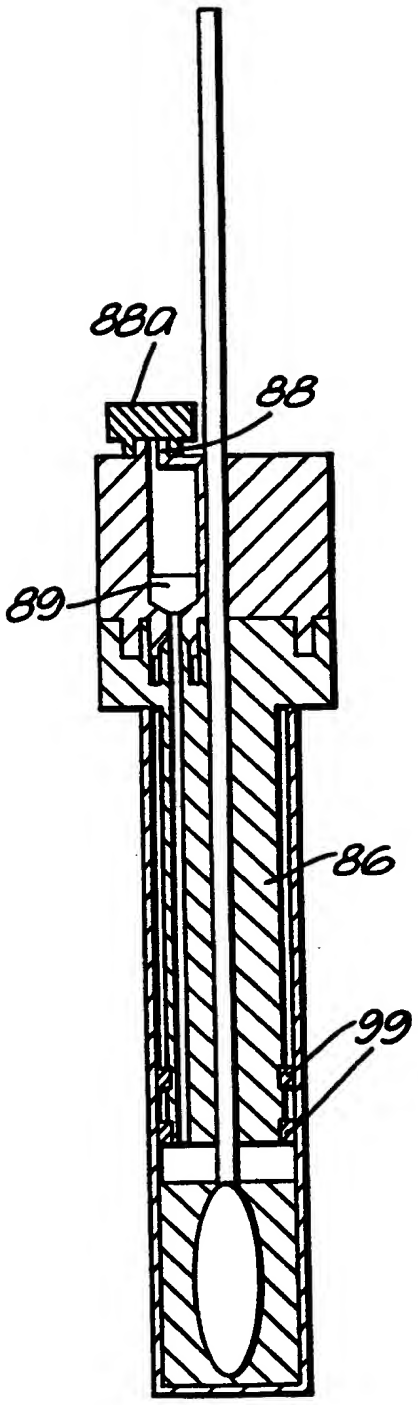


FIG. 19f



INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 93/01678

A. CLASSIFICATI N OF SUBJECT MATTER
IPC 5 G01N31/22 G01N33/52 //G01N33/569

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB,A,2 199 944 (CHRISTOPHER SONNEX) 20 July 1988 cited in the application	
A	DE,A,19 35 766 (DR. L. H. DAHL) 28 January 1971	
A	WO,A,89 07152 (UNIVERSITY COLLEGE CARDIFF CONSULTANTS LTD.) 10 August 1989	
A	WO,A,84 02923 (DAIRY AND FOOD LABS, INC.) 2 August 1984	
A	GB,A,1 234 044 (CONSOLIDATED LABORATORIES INC.) 3 June 1971	

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
17 November 1993	01. 12. 93

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 93/01678

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE WPI Week 8427, Derwent Publications Ltd., London, GB; AN 84-165497 E. MEHNERT 'PHOTOMETRIC DETERMN. OF NITROGEN CPDS. IN ORGANIC MATERIALS BY COLOUR REACTION WITH POTASSIUM TETRA:IODO-MERCURATE.' & DD,A,207 579 7 March 1984 see abstract	3,4

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 93/01678

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
GB-A-2199944	20-07-88	NONE		
DE-A-1935766	28-01-71	NONE		
WO-A-8907152	10-08-89	EP-A,B	0400086	05-12-90
		GB-A,B	2215044	13-09-89
		JP-T-	3503719	22-08-91
		US-A-	5124254	23-06-92
WO-A-8402923	02-08-84	AU-B-	573203	02-06-88
		AU-A-	2435884	15-08-84
		DE-A-	3376985	14-07-88
		EP-A,B	0134798	27-03-85
GB-A-1234044	03-06-71	NONE		